

Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1-26 (Cancelled).

27 (New). A method for screening a subject for schizophrenia, bipolar disorder and/or ADHD or a subject at risk of developing schizophrenia, bipolar disorder and/or ADHD, comprising either:

A) detecting a level of expression of at least one gene, selected from the group consisting of **(Table 1)**, in a sample of frontal pole tissue obtained from the subject to provide a first value, with the proviso that if expression of only one gene is detected that the gene is not any of the genes selected from the group consisting of **(Table 3)**; and

comparing the first value with a level of expression of the at least one gene in said detecting step in a sample of frontal pole tissue obtained from a disease-free subject, wherein a greater expression level in the subject sample compared to the sample from the disease-free subject of at least one gene with accession number X57514, U66707, AI639165, AF064868, or AI145494 or wherein a lower expression level in the subject sample compared to the sample from the disease-free subject of at least one gene with accession number U20643, H31232, S61973, ABO16160, X85184, J04063, S81353, M33025, AA858621, M74494, AA866358, M64986, AI227715, U77931, AA89392, AA859633, AA891969, AI145367, AA893711, Y09000, AA891940, D26564, AI101103, or AF014009 is indicative of the subject having schizophrenia, bipolar disorder and/or ADHD or at risk of developing schizophrenia, bipolar disorder and/or ADHD; or

B) detecting a level of expression of at least one gene, selected from the group consisting of **(Table 2)**, in a sample of hypothalamus tissue obtained from the subject to provide a first value, with the proviso that if expression of only one gene is detected that the gene is not any of the genes selected from the group consisting of **(Table 3)**; and

comparing the first value with a level of expression of the at least one gene in said detecting step in a sample of hypothalamus tissue obtained from a disease-free subject, wherein a greater expression level in the subject sample compared to the sample from the disease-free subject of at least one gene with accession number AA946532, AB016160, U57500, L17127,

M28648, L24776, AB020504, U77931, U75927, AF096269, AA892801, U49099, AA859597, AA875427, AF028784, L22760, AI014135, AI104513, AA894148, AI073204 or D38468, wherein a lower expression level in the subject sample compared to the sample from the disease-free subject of at least one gene with accession number M13100, M59980, M18331, M36418, X57764, U62897, S71570, M16112, AI008131, X12744, AI230260, U48245, U66707, H31692, D89863, X06564, M91234, U31554, AA875659, AA799421, AI014091, AB012234, U09793, AA800513, AI639381, AA799515, X83546, AI013194, AB008538, X52817, AA893065, H31588, AA859832, AI008074, AA851749, AA894321, AI227608, E13644, AA925762, M72422, M17526, U45479, U86635, AA894089, or AA891069 is indicative of the subject having schizophrenia, bipolar disorder and/or ADHD or at risk of developing schizophrenia, bipolar disorder and/or ADHD; or

C) detecting a level of expression of at least one gene, selected from the group consisting of **(Table 7)**, in a sample of frontal pole tissue obtained from the subject to provide a first value, with the proviso that if expression of only one gene is detected that the gene is not any of the genes selected from the group consisting of **(Table 3)**; and

comparing the first value with a level of expression of the at least one gene in said detecting step in a sample of frontal pole tissue obtained from a disease-free subject, wherein a greater expression level in the subject sample compared to the sample from the disease-free subject of at least one gene with accession number U66707, AA900582, AI012942, AF064868, AI044716, AF068136, X58865, AI179150, AA800881, K02248, AF001423, AI639157, AA891901, M30691, AI234950, X57514, S79523, AI639165, D00913, AJ224680, AA893711, AI639422, D14015, L31840, AF087674, X05472, AI145494, U77583, AA892797, U70268 or M88751 or wherein a lower expression level in the subject sample compared to the sample from the disease-free subject of at least one gene with accession number AA892376, AA866459, AA892483, AA891969, AJ001 641, AA799636, AA945054, AI008131, AA893670, AI227715, AA799576, AA799791, AA874982, X76489cds, Y09000, AA859663, U77931, AI145367, D10666, D38560, AB003992, AA859520, AB003991, AA894264, AA955388, X07729, M62752, AA799479, H32977, X54531, M64986, AA893164, M35300, AB016160 or AI101103 is indicative of the subject having schizophrenia, bipolar disorder and/or ADHD or at risk of developing schizophrenia, bipolar disorder and/or ADHD.

28 (New). The method of claim 27, wherein the level of expression of at least two genes, selected from the group consisting of **(Tables 1, 2 and 7)**, are detected.

29 (New). The method of claim 27 (A) or (B), wherein the at least one gene is selected

from the group consisting of genes with accession numbers: U20643, H31232, S61973, AB016160, X85184, J04063, S81353, M33025, X57514, AA858621, M74494, M13100, M59980, AA946532, M18331, M36418, X57764, U62897, U57500, L17127, S71570, M16112, AI008131, M28648, X12744, AI230260, U86635, and D38468.

30 (New). The method of claim 27, wherein the level of expression of the gene is determined by detecting the level of expression of a mRNA corresponding to the gene.

31 (New). The method of claim 30, wherein the level of expression of mRNA is detected by techniques selected from the group consisting of Microarray analysis, Northern blot analysis, reverse transcription PCR, and real time quantitative PCR.

32 (New). The method of claim 27, wherein the level of expression of the gene is determined by detecting the level of expression of a protein encoded by the gene.

33 (New). A method for monitoring the progression of schizophrenia, bipolar disorder, and/or ADHD in a subject having, or at risk of having, schizophrenia, bipolar disorder, and/or ADHD, comprising either:

A) measuring a level of expression of at least one gene, selected from the group consisting of **(Table 1)**, over time in the frontal pole tissue sample obtained from the subject with the proviso that if expression of only one gene is detected that the gene is not any of the genes selected from the group consisting of **(Table 3)**, wherein an increase in the level of expression of the at least one gene with accession number: X57514, U66707, AI639165, AF064868, or AI145494 over time is indicative of the progression of schizophrenia, bipolar disorder, and/or ADHD in the subject, or wherein a decrease in the level of expression of the at least one gene with accession number U20643, H31232, S61973, AB016160, X85184, J04063, S81353, M33025, AA858621, M74494, AA866358, M64986, AI227715, U77931, AA89392, AA859633, AA891969, AI145367, AA893711, Y09000, AA891940, D26564, AI101103, or AF014009 over time is indicative of the progression of schizophrenia, bipolar disorder, and/or ADHD in the subject; or

B) measuring a level of expression of at least one gene, selected from the group consisting of **(Table 2)**, over time in the hypothalamus tissue sample obtained from the subject with the proviso that if expression of only one gene is detected that the gene is not any of the genes selected from the group consisting of **(Table 3)**, wherein an increase in the level of expression of the at least one gene with accession number AA946532, AB016160, U57500, L17127, M28648, L24776, AB020504, U77931, U75927, AF096269, AA892801, U49099,

AA859597, AA875427, AF028784, L22760, AI014135, AI104513, AA894148, AI073204 or D38468 over time is indicative of the progression of schizophrenia, bipolar disorder, and/or ADHD in the subject, or wherein a decrease in the level of expression of the at least one gene with accession number M13100, M59980, M18331, M36418, X57764, U62897, S71570, M16112, AI008131, X12744, AI230260, U48245, U66707, H31692, D89863, X06564, M91234, U31554, AA875659, AA799421, AI014091, AB012234, U09793, AA800513, AI639381, AA799515, X83546, AI013194, AB008538, X52817, AA893065, H31588, AA859832, AI008074, AA851749, AA894321, AI227608, E13644, AA925762, M72422, M17526, U45479, U86635, AA894089, or AA891069 over time is indicative of the progression of schizophrenia, bipolar disorder, and/or ADHD in the subject.

34 (New). The method of claim 33, wherein the level of expression of at least two genes, selected from the group consisting of **(Table 1 and 2)**, are measured.

35 (New). The method of claim 33, wherein the at least one gene is selected from the group consisting of the genes with accession number U20643, H31232, S61973, AB016160, X85184, J04063, S81353, M33825, X57514, AA858621, M74494, M13100, M59980, AA946532, M18331, M36418, X57764, U62897, U57500, L17127, S71570, M16112, AI008131, M28648, X12744, AI230260, U86635, and D38468.

36 (New). A method for identifying agents for use in the treatment of schizophrenia, bipolar disorder, and for ADHD, comprising either:

- A. a) contacting a sample of cells expressing at least one gene selected from the group consisting of **(Tables 1 and 2)** with a candidate agent;
- b) detecting a level of expression of at least one gene in said cells, with the proviso that if expression of only one gene is detected that the gene is not any of the genes selected from the group consisting of **(Table 3)**; and
- c) comparing the level of expression of the at least one gene in the sample in the presence of the candidate agent with a level of expression of the at least one gene in cells that are not contacted with the candidate agent, wherein for genes with accession number U20643, H31232, S61973, X85184, J04063, S81353, M33025, AA858621, M74494, AA866358, M64986, AI227715, AA89392, AA859633, AA891969, AI145367, AA893711, Y09000, AA891940, D26564, AI101103, AF014009, M13100, M59980, M18331, M36418, X57764, U62897, S71570, M16112, AI008131, X12744, AI230260, U48245, H31692, D89863, X06564, M91234, U31554, AA875659, AA799421,

AI014091, AB012234, U09793, AA800513, AI639381, AA799515, X83546, AI013194, AB008538, X52817, AA893065, H31588, AA859832, AI008074, AA851749, AA894321, AI227608, E13644, AA925762, M72422, M17526, U45479, U86635, AA894089, or AA891069 an increased level of expression of the at least one gene in the sample in the presence of the candidate agent relative to the level of expression of the at least one gene in the sample in the absence of the candidate agent, or wherein for genes with accession number X57514, AI639165, AF064868, AI145494, AA946532, U57500, L17127, M28648, L24776, AB020504, U75927, AF096269, AA892801, U49099, AA859597, AA875427, AF028784, L22760, AI014135, AI104513, AA894148, AI073204 or D38468 a decreased level of expression of the at least one gene in the sample in the presence of the candidate agent relative to the level of expression of the at least one gene in the sample in the absence of the candidate agent and for genes with accession numbers AB016160 and U77931 an increased level of expression with respect to the frontal pole, and a decreased expression with respect to the hypothalamus and for a gene with accession number U66707 an increased expression with respect to hypothalamus and an decreased expression with respect to the frontal pole is indicative of an agent useful in the treatment of schizophrenia, bipolar disorder, and/or ADHD; or

- B.
- a) contacting a sample of cells expressing at least one gene, selected from the group consisting of **(Table 7)** with a candidate agent;
 - b) detecting level of expression of at least one gene in said cells with the proviso that if expression of only one gene is detected that the gene is not any of the genes selected from the group consisting of (Table 3); and
 - c) comparing the level of expression of the at least one gene in the sample in the presence of the candidate agent with a level of expression of the at least one gene in cells that are not contacted with the candidate agent, wherein for genes with accession number: AA892376, AA866459, AA892483, AA891969, AJ001641, AA799636, AA945054, AI008131, AA893670, AI227715, AA799576, AA799791, AA874982, X76489cds, Y09000, AA859663, U77931, AI145367, D10666, D38560, AB003992, AA859520, AB003991, AA894264, AA955388, X07729, M62752, AA799479, H32977, X54531, M64986, AA893164, M35300, AB016160 or AI101103 an increased level of expression of the at least one gene in the sample in the presence of the candidate agent relative to the level of expression of the at least one gene in the sample in the absence of the candidate agent: or wherein for genes with accession number: U66707, AA900582, AI012942, AF064868, AI044716, AF068136,

X58865, AI179150, AA800881, K02248, AF001423, AI639157, AA891901, M30691, AI234950, X57514, S79523, AI639165, D00913, AJ224680, AA893711, AI639422, D14015, L31840, AF087674, X05472, AI145494, U77583, AA892797, U70268 or M88751 a decreased level of expression of the at least one gene in the sample in the presence of the candidate agent relative to the level of expression of the at least one gene in the sample in the absence of the candidate agent; is indicative of an agent useful in the treatment of schizophrenia, bipolar disorder, and/or ADHD.

37 (New). The method of claim 36, wherein the level of expression of at least two genes in the sample is detected the detecting step (b).

38 (New). The method of claim 36(A), wherein the at least one gene is selected from the group consisting of genes with accession number U20643, H31232, S61973, AB016160, X85184, J04063, S81353, M33025, X57514, AA858621, M74494, M13100, M59980, AA946532, M18331, M36418, X57764, U62897, U57500, L17127, S71570, M16112, AI008131, M28648, X12744, AI230260, U86635, and D38468.

39 (New). A method of treating and preventing schizophrenia, bipolar disorder, and/or ADHD in patient in need thereof, comprising either:

A) administering to said patient an effective amount of an agent that can induce a decrease in the expression of at least one gene with accession number U66707, AA900582, AI012942, AF064868, AI044716, AF068136, X58865, AI179150, AA800881, K02248, AF001423, AI639157, AA891901, M30691, AI234950, X57514, S79523, AI639165, D00913, AJ224680, AA893711, AI639422, D14015, L31840, AF087674, X05472, AI145494, U77583, AA892797, U70268 and/or M88751; and/or induce an increase of at least one gene with accession number AA892376, AA866459, AA892483, AA891969, AJ001641, AA799636, AA945054, AI008131, AA893670, AI227715, AA799576, AA799791, AA874982, X76489cds, Y09000, AA859663, U77931, AI145367, DI0666, D38560, AB003992, AA859520, AB003991, AA894264, AA955388, X07729, M62752, AA799479, H32977, X54531, M64986, AA893164, M35300, AB016160 and/or for AI101103, with the proviso that if expression of only one gene is altered that the gene is not any selected from the group consisting of (**Table 3**); or

B) administering to said patient an effective amount of an agent that can induce a decrease in the expression of at least one gene with accession number X57514, AI639165, AF064868, AI145494, AA946532, U57500, L17127, L24776, A8020504, U75927, AF096269, AA892801, U49099, AA859597, AA875427, AF028784, L22760, AI014135, AI104513, AA894148, AI073204 and/or D38468; and/or induce an increase of at least one gene with

accession number U20643, H31232, S61973, X85184, J04063, S81353, M33025, AA858621, M74494, AA866358, M64986, AI227715, AA89392, AA859633, AA891969, AI145367, AA893711, Y09000, AA891940, D26564, AI101103, M28648, AF014009, MI3100, M59980, M18331, M36418, X57764, U62897, S71570, M16112, AI008131, X12744, AI230260, U48245, H31692, D89863, X06564, M91234, U31554, AA875659, AA799421, AI014091, AB012234, U09793, AA800513, AI639381, AA799515, X83546, AI03194, AB008538, X52817, AA893065, H31588, AA859832, AI008074, AA851749, AA894321, AI227608, E13644, AA925762, M72422, M17526, U45479, U86635, AA894089, and/or AA891069; and/or for genes AB016160 and/or U7793-lan increase with respect to frontal pole expression and a decrease to the hypothalamus expression; and/or for the gene U66707 a decrease with respect to the frontal pole and an increase with respect to the hypothalamus, with the proviso that if expression of only one gene is altered that the gene is not any gene of selected from the group consisting of **(Table 3)**.

40 (New). A method for monitoring the efficacy of a treatment of a subject having schizophrenia, bipolar disorder, and/or ADHD or at risk of developing schizophrenia, bipolar disorder, and/or ADHD with an agent, comprising either:

- A. a) obtaining a pre-administration sample in the frontal lobe from the subject prior to administration of the agent;
- b) detecting a level of expression of at least one gene, selected from the group consisting of **(Tables 1 and 7)**, in the pre-administration sample, with the proviso that if expression of only one gene is detected that the gene is not any gene selected from the group consisting of **(Table 3)**;
- c) obtaining one or more post-administration samples from the subject;
- d) detecting a level of expression of the at least one gene in the post-administration sample or samples;
- e) comparing the level of expression of the at least one gene in the pre-administration sample with the level of expression of the at least one gene in the post-administration sample; and
- f) adjusting the administration of the agent accordingly; or
- B. a) obtaining a pre-administration sample in the hypothalamus from the subject prior to administration of the agent;

- b) detecting a level of expression of at least one gene, selected from the group consisting of **(Table 2)**, in the pre-administration sample, with the proviso that if expression of only one gene is detected that the gene is not any gene selected from the group consisting of **(Table 3)**;
- c) obtaining one or more post-administration samples from the subject;
- d) detecting a level of expression of the at least one gene in the post-administration sample or samples;
- e) comparing the level of expression of the at least one gene in the pre-administration sample with the level of expression of the at least one gene in the post-administration sample; and
- f) adjusting the administration of the agent accordingly.

41 (New). The method of claim 40, wherein the level of expression of at least two genes, selected from the group consisting of **(Tables 1, 2 and 7)**, is detected in step (b).

42 (New). The method of claim 40, wherein the level of expression of mRNA is detected by techniques selected from the group consisting of Microarray analysis, Northern blot analysis, reverse transcription PCR and real time quantitative PCR.

43 (New). A transgenic mouse whose genome comprises a disruption of any of the endogenous genes selected from the group consisting of **(Table 1, 2 and 7)**, wherein said disruption comprises the insertion of a transgene, and wherein said disruption results in said transgenic mouse not exhibiting normal expression of any of said endogenous genes with the proviso that if only one gene is disrupted it is not one of the genes of selected from the group consisting of **(Table 3)**.

44 (New). A method for producing a rodent having schizophrenia, bipolar disorder, and/or ADHD or at risk of developing schizophrenia, bipolar disorder, and/or ADHD, comprising subjecting the rodent to variable repeated stress during the last week of the gestation, starting on embryonic day 14 and continuing until the natural delivery of a pup at about embryonic day 22.